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Study Profile

Rationale, design, and profile of the Three-Prefecture Cohort in Japan: A 15-year follow-up



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ABSTRACT

Background: We reutilized the existing Three-Prefecture Cohort to evaluate the relationship between lifestyle factors and the incidence or mortality from non-communicable diseases.

Methods: This study was a prospective population-based observation conducted from the 1980s to 2000 in three prefectures (Miyagi, Aichi, and Osaka) in Japan. The study subjects were residents aged ≥ 40 years who received a questionnaire. The follow-up period was 15 years from the baseline survey in each study area. A self-administered questionnaire, which included items on participants' demographic factors and lifestyle characteristics, was administered. Vital status and date of death were collected from residence certificates by the local government, and cause of death was identified using vital statistics. Cancer incidence and the date of diagnosis were collected from local cancer registry data.

Results: A total of 46,421 men and 54,189 women were eligible for our analysis. The person-years of follow-up for cancer incidence were 464,664 and 567,271 for men and women, respectively, and those for death were 527,940 and 648,601 for men and women, respectively. There were 8479 cancer incidences (5106 men and 3373 women) and 20,240 total deaths (11,156 men and 9084 women). The stomach was the most common cancer incidence site for both men (25.6%) and women (18.6%). The leading cause of death was cancer among men (35.0%) and cardiovascular disease among women (41.0%).

Conclusions: The Three-Prefecture Cohort Study enabled us to reveal the association of multiphasic lifestyle factors with cancer incidence and mortality. The study will also allow us to conduct a pooled analysis in combination with other large-scale cohorts.

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Introduction

A cohort study is one of the ways to evaluate the relationship between lifestyle factors and the incidence or mortality from non-

communicable diseases. Although huge amounts of money and long-term observation are needed to conduct a cohort study, such a design could minimize selection bias and maximized external validity. Large-scale prospective cohorts focused on healthy populations (e.g., the Japan Collaborative Cohort [JACC] Study¹ or the Japan Public Health-Based Prospective Cohort [JPHC] Study²) have been conducted since 1980s in Japan. There have also been large cohort studies worldwide, such as the National Institutes of Health–American Association of Retired Persons Diet and Health

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Table 1
Participants of the Three-Prefecture Cohort study.

| | Miyagi Prefecture | | Aichi Prefecture | | Osaka Prefecture | | Total |
|--|---|---------------------------------------|---|---------------------------------------|----------------------------------|--|---------|
| | Sendai-City (6 areas in Aoba and Miyagino wards) | Wakuya/Tajiri-Towns (Entire towns) | Nagoya-City (5 areas in Chigusa ward) | Inuyama-City (2 areas in the city) | Osaka-City (Higashinari ward) | Nose/Kanan/Kumatori-Town (Entire towns) | |
| All residents aged ≥ 40 years old | 25,237 | 15,891 | 24,489 | 12,854 | 39,307 | 21,230 | 139,008 |
| Delivered questionnaires | 17,805 | 14,926 | 23,331 | 12,815 | 27,051 | 21,101 | 117,029 |
| Responded questionnaires | 17,195 | 14,574 | 21,535 | 12,003 | 20,665 | 18,565 | 104,537 |
| Response rate (%) ^a | (68.1) | (91.7) | (87.9) | (93.4) | (52.6) | (87.4) | (75.2) |
| Response rate (%) ^b | (96.6) | (97.6) | (92.3) | (93.7) | (76.4) | (88.0) | (89.3) |

^a Denominator was subjects who were all residents aged ≥ 40 years old.^b Denominator was subjects who were delivered the self-administrated questionnaire.

Study in the United States,³ the European Prospective Investigation into Cancer and Nutrition in Europe,⁴ and the Korean Multi-center Cancer Cohort Study in Korea.⁵ Indeed, many findings have been obtained from these studies.

The Three-Prefecture Cohort Study was a prospective population-based observational study launched in 1983, which targeted approximately 100,000 inhabitants in Miyagi Prefecture, Aichi Prefecture, and Osaka Prefecture in Japan and conducted a questionnaire survey to reveal the association of multiphasic life-style factors with cancer incidence or mortality. Here, we briefly described the study concept and the cohort population's profile.

Materials and methods

Study design and settings

This cohort, which has been under prospective observation since 1983, was studied to assess the long-term effects of air pollution on mortality from lung cancer and respiratory diseases.^{6,7} The study areas were chosen because they contained a national air monitoring station and had well-managed cancer surveillance systems in 1983, including eight selected urban/rural areas in Miyagi Prefecture (Sendai City and Wakuya/Tajiri Town), Aichi

Prefecture (Nagoya City and Inuyama City), and Osaka Prefecture (Osaka City and Nose/Kanan/Kumatori Town). Since the 1970s, there has been a network of ambient air monitoring stations in Japan operated by the Ministry of Environment (formerly the National Environment Agency) and local governments. In this study, we defined rural areas as cities/towns with general air pollution monitoring stations (control area) and urban areas as cities/towns with automobile exhaust gas measurement stations (pollution area).⁶ Self-administered questionnaires in sealed envelopes were distributed by hand to targeted individuals in cooperation with the municipal government in each area and were collected after a set period of time. The study committee, consisting of health center directors, local officials, and residents' association representatives, was established to protect personal information of the participants and ensure the accuracy of the study. In this study, we merged individuals' data with their cancer incidence information based on personal name, gender, and date of birth. The proportion of death certificate only (DCO) deaths in each area was 9.1%–17.8% in Miyagi Prefecture,⁸ 28.1%–32.6% in Aichi Prefecture,⁹ and 20.7%–23.4% in Osaka Prefecture.¹⁰

The study subjects were residents aged ≥ 40 years who received a questionnaire, and they were enrolled between 1983 and 1985. The investigation was begun in Osaka Prefecture in 1983, in Miyagi

Table 2
Distribution of cohort participants at baseline by gender, age, and region.

| | Age at baseline, years | | | | | | | | | | Total | % |
|---------------------------------------|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-----|--------|-------|
| | 40–44 | 45–49 | 50–54 | 55–59 | 60–64 | 65–69 | 70–74 | 75–79 | 80–84 | ≥85 | | |
| Men | | | | | | | | | | | | |
| Japan census population 1985 (x1,000) | 4494 | 4053 | 3898 | 3391 | 2349 | 1771 | 1486 | 997 | 546 | 247 | 23,232 | |
| % | 19.3 | 17.4 | 16.8 | 14.6 | 10.1 | 7.6 | 6.4 | 4.3 | 2.4 | 1.1 | | 100.0 |
| Three-prefecture cohort participants | 8082 | 7735 | 7795 | 6804 | 5018 | 4067 | 3410 | 2153 | 973 | 384 | 46,421 | |
| % | 17.4 | 16.7 | 16.8 | 14.7 | 10.8 | 8.8 | 7.3 | 4.6 | 2.1 | 0.8 | | 100.0 |
| Miyagi Prefecture (urban) | 1137 | 1161 | 1194 | 1057 | 859 | 765 | 586 | 371 | 189 | 72 | 7391 | 15.9 |
| Miyagi Prefecture (rural) | 903 | 1020 | 1213 | 1082 | 784 | 607 | 490 | 333 | 116 | 53 | 6601 | 14.2 |
| Aichi Prefecture (urban) | 1841 | 1821 | 1760 | 1358 | 1035 | 818 | 675 | 442 | 220 | 74 | 10,044 | 21.6 |
| Aichi Prefecture (rural) | 1095 | 989 | 963 | 823 | 561 | 476 | 377 | 250 | 109 | 49 | 5692 | 12.3 |
| Osaka Prefecture (urban) | 990 | 1161 | 1265 | 1183 | 927 | 764 | 718 | 440 | 193 | 67 | 7708 | 16.6 |
| Osaka Prefecture (rural) | 2116 | 1583 | 1400 | 1301 | 852 | 637 | 564 | 317 | 146 | 69 | 8985 | 19.4 |
| Women | | | | | | | | | | | | |
| Japan census population 1985 (x1,000) | 4554 | 4140 | 3971 | 3574 | 3011 | 2394 | 2046 | 1438 | 906 | 525 | 26,559 | |
| % | 17.1 | 15.6 | 15.0 | 13.5 | 11.3 | 9.0 | 7.7 | 5.4 | 3.4 | 2.0 | | 100.0 |
| Three-prefecture cohort participants | 8522 | 8522 | 8337 | 7814 | 6604 | 5196 | 4261 | 2722 | 1471 | 740 | 54,189 | |
| % | 15.7 | 15.7 | 15.4 | 14.4 | 12.2 | 9.6 | 7.9 | 5.0 | 2.7 | 1.4 | | 100.0 |
| Miyagi Prefecture (urban) | 1318 | 1447 | 1508 | 1379 | 1234 | 937 | 740 | 453 | 257 | 110 | 9383 | 17.3 |
| Miyagi Prefecture (rural) | 938 | 1161 | 1354 | 1268 | 1009 | 758 | 717 | 391 | 220 | 154 | 7970 | 14.7 |
| Aichi Prefecture (urban) | 1911 | 1944 | 1785 | 1621 | 1361 | 1020 | 843 | 578 | 264 | 141 | 11,468 | 21.2 |
| Aichi Prefecture (rural) | 1071 | 1050 | 897 | 869 | 711 | 638 | 459 | 346 | 171 | 94 | 6306 | 11.6 |
| Osaka Prefecture (urban) | 1264 | 1380 | 1404 | 1377 | 1246 | 1031 | 820 | 501 | 291 | 125 | 9439 | 17.4 |
| Osaka Prefecture (rural) | 2020 | 1540 | 1389 | 1300 | 1043 | 812 | 682 | 453 | 268 | 116 | 9623 | 17.8 |

Table 3

Selected baseline demographic and lifestyle characteristics of participants by gender.

| | Men (n = 46,421) | Women (n = 54,189) |
|---|---------------------|-----------------------|
| Mean age, years (standard deviation) | 56.1 (11.2) | 57.1 (11.6) |
| Regions, n (%) | | |
| Miyagi, urban | 7391 (15.9) | 9383 (17.3) |
| Miyagi, rural | 6601 (14.2) | 7970 (14.7) |
| Aichi, urban | 10,044 (21.6) | 11,468 (21.2) |
| Aichi, rural | 5692 (12.3) | 6306 (11.6) |
| Osaka, urban | 7708 (16.6) | 9439 (17.4) |
| Osaka, rural | 8985 (19.4) | 9623 (17.8) |
| Health insurance type, n (%) | | |
| National health insurance | 20,877 (45.0) | 25,263 (46.6) |
| Government/union-managed health insurance | 19,267 (41.5) | 20,864 (38.5) |
| Mutual aid associations health insurance | 3897 (8.4) | 4250 (7.8) |
| Others | 577 (1.2) | 891 (1.6) |
| Missing | 1803 (3.9) | 2921 (5.4) |
| History of hypertension, n (%) | | |
| Current | 8289 (17.9) | 10,138 (18.7) |
| Past | 1709 (3.7) | 2189 (4.0) |
| Never | 19,820 (42.7) | 23,811 (43.9) |
| Missing | 16,603 (35.8) | 18,051 (33.3) |
| History of diabetes, n (%) | | |
| Current | 2725 (5.9) | 1803 (3.3) |
| Past | 738 (1.6) | 275 (0.5) |
| Never | 20,895 (45.0) | 25,586 (47.2) |
| Missing | 22,063 (47.5) | 26,525 (48.9) |
| Body mass index, n (%) | | |
| ≤19.0 kg/m ² | 4310 (9.3) | 6255 (11.5) |
| 19.0–21.9 kg/m ² | 14,995 (32.3) | 17,153 (31.7) |
| 22.0–24.9 kg/m ² | 17,155 (37.0) | 17,294 (31.9) |
| 25.0–29.9 kg/m ² | 7528 (16.2) | 9378 (17.3) |
| ≥30.0 kg/m ² | 515 (1.1) | 1130 (2.1) |
| Missing | 1918 (4.1) | 2979 (5.5) |
| Alcohol drinking, n (%) | | |
| Never | 7122 (15.3) | 26,119 (48.2) |
| Former | 2787 (6.0) | 1094 (2.0) |
| Current occasional | 11,884 (25.6) | 13,497 (24.9) |
| Current almost daily | 21,776 (46.9) | 2942 (5.4) |
| Missing | 2852 (6.1) | 10,537 (19.4) |
| Smoking status, n (%) | | |
| Never | 7411 (16.0) | 37,281 (68.8) |
| Former | 10,805 (23.3) | 1746 (3.2) |
| Current | 23,969 (51.6) | 5199 (9.6) |
| Missing | 4236 (9.1) | 9963 (18.4) |
| Green and yellow vegetable consumption, n (%) | | |
| ≤1–2 times/month | 3311 (7.1) | 2183 (4.0) |
| 1–2 times/week | 10,320 (22.2) | 8563 (15.8) |
| 3–4 times/week | 12,623 (27.2) | 14,918 (27.5) |
| Almost daily | 17,509 (37.7) | 24,445 (45.1) |
| Missing | 2658 (5.7) | 4080 (7.5) |
| Non-green and non-yellow vegetable consumption, n (%) | | |
| ≤1–2 times/month | 1491 (3.2) | 1111 (2.1) |
| 1–2 times/week | 6634 (14.3) | 5229 (9.6) |
| 3–4 times/week | 12,267 (26.4) | 12,816 (23.7) |
| Almost daily | 23,782 (51.2) | 31,276 (57.7) |
| Missing | 2247 (4.8) | 3757 (6.9) |
| Fruit consumption, n (%) | | |
| ≤1–2 times/month | 5040 (10.9) | 2452 (4.5) |
| 1–2 times/week | 9631 (20.7) | 6291 (11.6) |
| 3–4 times/week | 10,303 (22.2) | 10,649 (19.7) |
| Almost daily | 18,308 (39.4) | 30,535 (56.3) |
| Missing | 3139 (6.8) | 4262 (7.9) |
| Miso soup consumption, n (%) | | |
| ≤1–2 times/month | 3141 (6.8) | 3823 (7.1) |
| 1–2 times/week | 7127 (15.4) | 8473 (15.6) |
| 3–4 times/week | 8035 (17.3) | 9746 (18.0) |
| Almost daily | 25,913 (55.8) | 28,213 (52.1) |
| Missing | 2205 (4.8) | 3934 (7.3) |
| Pickled vegetable consumption, n (%) | | |
| Scarcely any | 2296 (4.9) | 2095 (3.9) |
| 1–2 times/month | 2311 (5.0) | 2380 (4.4) |
| 1–2 times/week | 5114 (11.0) | 5340 (9.9) |
| 3–4 times/week | 6508 (14.0) | 6753 (12.5) |
| Almost daily | 27,016 (58.2) | 32,802 (60.5) |

Table 3 (continued)

| | Men (n = 46,421) | Women (n = 54,189) |
|--|---------------------|-----------------------|
| Missing | 3176 (6.8) | 4819 (8.9) |
| Type of job, n (%) | | |
| Professional technical and civil workers | 3835 (8.3) | 2805 (5.2) |
| Managerial workers | 959 (2.1) | 98 (0.2) |
| Clerical workers | 5415 (11.7) | 5197 (9.6) |
| Sales workers | 5495 (11.8) | 3663 (6.8) |
| Agricultural, forestry and fisheries workers | 2844 (6.1) | 3127 (5.8) |
| Construction workers | 92 (0.2) | 9 (0.0) |
| Workers in transport and communications | 1814 (3.9) | 309 (0.6) |
| Craftsman, production process worker, and laborers | 9537 (20.5) | 4740 (8.7) |
| Workers in security | 567 (1.2) | 18 (0.0) |
| Service workers | 1069 (2.3) | 2750 (5.1) |
| Unemployed | 1284 (2.8) | 10,666 (19.7) |
| Missing | 13,510 (29.1) | 20,807 (38.4) |

Prefecture in 1984, and in Aichi Prefecture in 1985. The number of questionnaire responders was 17,195/17,805 (96.6%) in Sendai City, 14,574/14,926 (97.6%) in Wakuya/Tajiri Town, 21,535/23,331 (92.3%) in Nagoya City, 12,003/12,815 (93.7%) in Inuyama City, 20,665/27,051 (76.4%) in Osaka City, and 18565/21,101 (88.0%) in Nose/Kanan/Kumatori Town (Table 1). Of 104,537 responders, a total of 100,629 were included as subjects, after excluding those who answered a questionnaire in duplicate or did not provide their name/gender/date of birth because investigators could not follow up the outcome data in the Three-Prefecture Cohort study.

Questionnaire

Baseline questionnaire items included the following: area of residence, gender, height, weight, health condition at that time, past medical history, type of insurance, health check-up/cancer screening history, frequency of food intake, smoking, alcohol drinking status, parent's medical history, smoking status of co-habitants, house environment, occupation (such as the longest period of employment), and reproductive history (only for women). Medical history included: past history of diabetes mellitus, hypertension, stroke, and emphysema; and stomach cancer screening by x-ray examination, blood pressure measurement, and uterus cancer screening (only for women). Food intake frequency of items, such as rice, bread, meat, fish, eggs, milk, green/yellow vegetables, non-green/yellow vegetables, fruit, miso soup, and pickled vegetables, as well as drinking beverages, such as green tea, black tea, and coffee, was assessed categorically.

Follow-up

The follow-up period was defined as 15 years from the baseline survey in each study area, except for cancer incidence data in Miyagi Prefecture, for which follow-up was 9 years. The cohorts were followed from 1984 to 1999 in Miyagi Prefecture, from 1985 to 2000 in Aichi Prefecture, and from 1983 to 2000 in Osaka Prefecture. Vital status, date of death, and date of move-out from the study area were confirmed by the local government using residence certificates. Cause of death was identified using death certificate. Cancer incidence and the date of diagnosis were collected from local cancer registry data.

Statistical analysis

The definition of disease was determined based on the International Classification of Diseases 9th version (ICD-9) for data

collected from 1983 to 1994 and or the 10th version (ICD-10) for data collected from 1995 to 2000 in this study. We counted the number of incident cancers and deaths of all cancer and cancer of individual sites, and also the number of deaths according to cause of death. When mortality rates were calculated, person-years of follow-up for mortality were counted from the date of the baseline survey to the date of death, date of move-out from the study area, or the end of 15-year follow-up (whichever occurred first). For cancer incidence rates, date of diagnosis of first primary cancer was added to the above list. In addition, standardized incidence ratios (SIRs) and standardized mortality ratios (SMRs) of all-cause and all cancer were calculated using age-adjusted mortality/incidence rate, which was calculated using 5-year age-specific rates in each year according to the cancer registry and vital statistics in Japan.^{11,12} Statistical analyses were implemented using STATA version 13 MP (Stata Corp., College Station, TX, USA).

Ethics

The study was approved by the institutional review board of the National Cancer Center and the Ethics Committee of Osaka University School of Medicine. We received permission from the municipal governments to survey residents. The response to the questionnaire by participant was considered consent to participate in the survey. Tohoku University, Aichi Cancer Center, and Osaka Medical Center for Cancer and Cardiovascular Diseases were primarily responsible for analyzing information on baseline surveys, linking with cancer incidence and cause of death data, and altering the data set to unlinkable anonymized data. Although the National Cancer Center had originally managed the integrated datasets, Osaka University manages them at present. In the Three-Prefecture

Cohort study, researchers only analyzed unlinkable anonymous data.

Results

Of 100,629 participants aged 40–99 years old at baseline, 19 (0.02%) were excluded because their responses preceded the date of beginning of follow-up, which was unified in each area after various dates of individual response to the questionnaire. As a result, 46,421 men and 54,189 women were eligible for this study. Details of the distribution of cohort participants at baseline by sex, age, and region are noted in Table 2. The person-years of follow-up for cancer incidence were 464,664 and 567,271 for men and women, respectively, and the person-years for death were 527,940 and 648,601 for men and women, respectively.

Table 3 shows selected baseline characteristics of participants by sex. Mean age among men and women was 56.1 and 57.1 years, respectively, and the proportion of participants with a body mass index of 22.0–24.9 kg/m² was 37.0% among men and 31.9% among women. The proportion of current drinkers of alcoholic beverages was 46.9% for men and 5.4% for women, and the proportion of current smokers was 51.6% for men and 9.6% for women. Regarding the longest period occupational classification, the proportion of participants engaged in clerical work was 11.7% among men and 9.6% among women, and the proportion of those unemployed was 2.8% among men and 19.7% among women.

Table 4 shows the follow-up results, Table 5 lists major types of incident cancers, and Table 6 lists major causes of death by gender. There were 20,240 total deaths (20.1%; 11,156 men and 9084 women), and 20,281 move-outs (20.2%; 9145 men and 11,136 women) (Table 4). The SIR of all cancers was 0.96 among men and

Table 4
15-year follow-up status until 2000 by gender and age.

| | Age at baseline, years | | | | | | | | | | Total |
|--|------------------------|---------|---------|---------|--------|--------|--------|--------|-------|-------|---------|
| | 40–44 | 45–49 | 50–54 | 55–59 | 60–64 | 65–69 | 70–74 | 75–79 | 80–84 | ≥85 | |
| Men | | | | | | | | | | | |
| Number at baseline | 8082 | 7735 | 7795 | 6804 | 5018 | 4067 | 3410 | 2153 | 973 | 384 | 46,421 |
| Number of all cancer incidences | 215 | 371 | 665 | 891 | 841 | 802 | 712 | 414 | 159 | 36 | 5106 |
| % (Number of all cancer incidences/Number at baseline) | 2.7 | 4.8 | 8.5 | 13.1 | 16.8 | 19.7 | 20.9 | 19.2 | 16.3 | 9.4 | 11.0 |
| Number of deaths | 320 | 506 | 960 | 1268 | 1407 | 1790 | 2054 | 1642 | 850 | 359 | 11,156 |
| % (Number of all cause deaths/Number at baseline) | 4.0 | 6.5 | 12.3 | 18.6 | 28.0 | 44.0 | 60.2 | 76.3 | 87.4 | 93.5 | 24.0 |
| Number of all cancer deaths | 135 | 230 | 463 | 642 | 615 | 641 | 626 | 375 | 140 | 35 | 3902 |
| % (Number of all cancer deaths/Number at baseline) | 1.7 | 3.0 | 5.9 | 9.4 | 12.3 | 15.8 | 18.4 | 17.4 | 14.4 | 9.1 | 8.4 |
| Number who left study area | 2359 | 1991 | 1608 | 1151 | 735 | 558 | 421 | 226 | 80 | 16 | 9145 |
| % (Number who left study area/Number at baseline) | 29.2 | 25.7 | 20.6 | 16.9 | 14.6 | 13.7 | 12.3 | 10.5 | 8.2 | 4.2 | 19.7 |
| Person-years (incidence) | 87,758 | 83,560 | 83,345 | 71,783 | 50,831 | 37,773 | 28,223 | 14,550 | 5175 | 1666 | 464,664 |
| Incidence rate (all cancer per 1000 person-years) | 2.4 | 4.4 | 8.0 | 12.4 | 16.5 | 21.2 | 25.2 | 28.5 | 30.7 | 21.6 | 11.0 |
| Person-years (mortality) | 96,389 | 93,649 | 95,428 | 83,102 | 59,579 | 44,107 | 32,193 | 16,278 | 5500 | 1714 | 527,940 |
| Mortality rate (all cause per 1000 person-years) | 3.3 | 5.4 | 10.1 | 15.3 | 23.6 | 40.6 | 63.8 | 100.9 | 154.5 | 209.4 | 21.1 |
| Mortality rate (all cancer per 1000 person-years) | 1.4 | 2.5 | 4.9 | 7.7 | 10.3 | 14.5 | 19.4 | 23.0 | 25.5 | 20.4 | 7.4 |
| Women | | | | | | | | | | | |
| Number at baseline | 8522 | 8522 | 8337 | 7814 | 6604 | 5196 | 4261 | 2722 | 1471 | 740 | 54,189 |
| Number of cancer incidences | 229 | 291 | 386 | 483 | 513 | 539 | 478 | 296 | 121 | 37 | 3373 |
| % (Number of all cancer incidences/Number at baseline) | 2.7 | 3.4 | 4.6 | 6.2 | 7.8 | 10.4 | 11.2 | 10.9 | 8.2 | 5.0 | 6.2 |
| Number of deaths | 181 | 301 | 446 | 662 | 946 | 1365 | 1712 | 1648 | 1157 | 666 | 9084 |
| % (Number of all cause deaths/Number at baseline) | 2.1 | 3.5 | 5.3 | 8.5 | 14.3 | 26.3 | 40.2 | 60.5 | 78.7 | 90.0 | 16.8 |
| Number of all cancer deaths | 98 | 170 | 211 | 286 | 325 | 410 | 404 | 278 | 115 | 34 | 2331 |
| % (Number of all cancer deaths/Number at baseline) | 1.1 | 2.0 | 2.5 | 3.7 | 4.9 | 7.9 | 9.5 | 10.2 | 7.8 | 4.6 | 4.3 |
| Number who left study area | 2242 | 2051 | 1693 | 1483 | 1233 | 1012 | 758 | 440 | 166 | 58 | 11,136 |
| % (Number who left study area/Number at baseline) | 26.3 | 24.1 | 20.3 | 19.0 | 18.7 | 19.5 | 17.8 | 16.2 | 11.3 | 7.8 | 20.6 |
| Person-years (incidence) | 94,984 | 94,636 | 92,190 | 85,763 | 71,427 | 53,084 | 40,224 | 22,468 | 9322 | 3172 | 567,271 |
| Incidence rate (all cancer per 1000 person-years) | 2.4 | 3.1 | 4.2 | 5.6 | 7.2 | 10.2 | 11.9 | 13.2 | 13.0 | 11.7 | 5.9 |
| Person-years (mortality) | 105,776 | 107,461 | 107,287 | 100,096 | 83,052 | 60,982 | 46,008 | 24,740 | 9927 | 3272 | 648,601 |
| Mortality rate (all cause per 1000 person-years) | 1.7 | 2.8 | 4.2 | 6.6 | 11.4 | 22.4 | 37.2 | 66.6 | 116.6 | 203.5 | 14.0 |
| Mortality rate (all cancer per 1000 person-years) | 0.9 | 1.6 | 2.0 | 2.9 | 3.9 | 6.7 | 8.8 | 11.2 | 11.6 | 10.4 | 3.6 |

Table 5

Distribution of number of cancer incidence by site, gender, and age at baseline during 15-year follow-up.

| ICD10 | ICD9 | | Age at baseline, years | | | | | | | | | | Total | % |
|---------|-------------|--|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-----|-------|-------|
| | | | 40–44 | 45–49 | 50–54 | 55–59 | 60–64 | 65–69 | 70–74 | 75–79 | 80–84 | ≥85 | | |
| Men | | | | | | | | | | | | | | |
| C00–C97 | 140–208.9 | all cancer | 215 | 371 | 665 | 891 | 841 | 802 | 712 | 414 | 159 | 36 | 5106 | 100.0 |
| C15 | 150–150.9 | Esophagus | 14 | 20 | 25 | 43 | 35 | 29 | 29 | 8 | 4 | 0 | 207 | 4.1 |
| C16 | 151–151.9 | Stomach | 52 | 94 | 180 | 235 | 224 | 191 | 187 | 95 | 34 | 10 | 1302 | 25.5 |
| C18 | 153–153.9 | Colon | 26 | 40 | 78 | 74 | 75 | 75 | 52 | 37 | 19 | 1 | 477 | 9.3 |
| C19–20 | 154–154.9 | Rectum | 18 | 28 | 29 | 44 | 46 | 33 | 23 | 21 | 3 | 1 | 246 | 4.8 |
| C22 | 155–155.9 | Liver and intrahepatic bile ducts | 24 | 58 | 117 | 137 | 82 | 83 | 57 | 33 | 15 | 2 | 608 | 11.9 |
| C23 | 156 | Gall bladder | 0 | 2 | 3 | 3 | 2 | 3 | 4 | 2 | 0 | 0 | 19 | 0.4 |
| C24 | 156.1–156.9 | Other and unspecified parts of biliary tract | 4 | 4 | 11 | 9 | 11 | 20 | 15 | 8 | 4 | 2 | 88 | 1.7 |
| C25 | 157–157.9 | Pancreas | 10 | 10 | 19 | 34 | 37 | 33 | 29 | 21 | 8 | 2 | 203 | 4.0 |
| C33–34 | 162–162.9 | Lung | 24 | 38 | 79 | 120 | 160 | 174 | 160 | 85 | 25 | 8 | 873 | 17.1 |
| C61 | 185–185.9 | Prostate | 1 | 7 | 10 | 39 | 31 | 41 | 35 | 25 | 15 | 2 | 206 | 4.0 |
| C64 | 189–189.1 | Kidney | 3 | 10 | 8 | 21 | 14 | 11 | 8 | 7 | 0 | 0 | 82 | 1.6 |
| C65–67 | 189.2–189.4 | Urothelial tract | 2 | 9 | 4 | 11 | 9 | 13 | 11 | 3 | 2 | 0 | 64 | 1.3 |
| C82–85 | 202–202.9 | Non-Hodgkin's | 3 | 5 | 10 | 10 | 12 | 7 | 8 | 5 | 2 | 3 | 65 | 1.3 |
| | 200–200.9 | | | | | | | | | | | | | |
| C90 | 203–203.8 | Multiple myeloma | 1 | 0 | 5 | 3 | 8 | 3 | 0 | 3 | 1 | 0 | 24 | 0.5 |
| C92 | 205–205.9 | Myeloid leukemia | 4 | 3 | 7 | 6 | 5 | 7 | 3 | 3 | 1 | 2 | 41 | 0.8 |
| Women | | | | | | | | | | | | | | |
| C00–C97 | 140–208.9 | all cancer | 229 | 291 | 386 | 483 | 513 | 539 | 478 | 296 | 121 | 37 | 3373 | 100.0 |
| C15 | 150–150.9 | Esophagus | 0 | 1 | 1 | 4 | 4 | 5 | 5 | 5 | 0 | 0 | 25 | 0.7 |
| C16 | 151–151.9 | Stomach | 32 | 49 | 59 | 83 | 104 | 103 | 96 | 63 | 35 | 6 | 630 | 18.7 |
| C18 | 153–153.9 | Colon | 10 | 35 | 44 | 54 | 53 | 67 | 59 | 41 | 12 | 6 | 381 | 11.3 |
| C19–20 | 154–154.9 | Rectum | 15 | 15 | 24 | 25 | 29 | 28 | 27 | 11 | 10 | 2 | 186 | 5.5 |
| C22 | 155–155.9 | Liver and intrahepatic bile ducts | 5 | 14 | 22 | 31 | 38 | 43 | 29 | 11 | 8 | 2 | 203 | 6.0 |
| C23 | 156 | Gall bladder | 0 | 3 | 3 | 3 | 5 | 5 | 4 | 6 | 0 | 0 | 29 | 0.9 |
| C24 | 156.1–156.9 | Other and unspecified parts of biliary tract | 2 | 3 | 5 | 8 | 12 | 21 | 16 | 13 | 5 | 2 | 87 | 2.6 |
| C25 | 157–157.9 | Pancreas | 3 | 6 | 9 | 26 | 25 | 35 | 28 | 19 | 5 | 1 | 157 | 4.7 |
| C33–34 | 162–162.9 | Lung | 16 | 8 | 26 | 42 | 52 | 56 | 60 | 34 | 10 | 5 | 309 | 9.2 |
| C50 | 174–175.9 | Breast | 72 | 74 | 71 | 73 | 58 | 42 | 30 | 13 | 6 | 0 | 439 | 13.0 |
| C53 | 180–180.9 | Cervi uteri | 16 | 17 | 8 | 22 | 15 | 14 | 17 | 8 | 1 | 0 | 118 | 3.5 |
| C54 | 182–182.9 | Corpus uteri | 9 | 13 | 22 | 15 | 7 | 8 | 4 | 0 | 0 | 0 | 78 | 2.3 |
| C55 | 184–184.9 | Uterus, part unspecified | 0 | 0 | 1 | 1 | 2 | 3 | 1 | 1 | 2 | 0 | 11 | 0.3 |
| C56 | 183–183.9 | Ovary | 15 | 13 | 18 | 12 | 8 | 10 | 12 | 7 | 4 | 0 | 99 | 2.9 |
| C64 | 189–189.1 | Kidney | 2 | 1 | 4 | 3 | 2 | 2 | 5 | 1 | 3 | 0 | 23 | 0.7 |
| C65–67 | 189.2–189.4 | Urothelial tract | 0 | 0 | 4 | 3 | 5 | 7 | 3 | 3 | 0 | 1 | 26 | 0.8 |
| C82–85 | 200–200.9 | Non-Hodgkin's | 2 | 3 | 4 | 10 | 7 | 6 | 6 | 5 | 4 | 1 | 48 | 1.4 |
| | 202–202.9 | | | | | | | | | | | | | |
| C90 | 203–203.8 | Multiple myeloma | 0 | 0 | 3 | 4 | 4 | 4 | 6 | 3 | 1 | 1 | 26 | 0.8 |
| C92 | 205–205.9 | Myeloid leukemia | 4 | 5 | 3 | 4 | 3 | 6 | 1 | 2 | 0 | 0 | 28 | 0.8 |

1.22 among women. The SMR of all causes was 0.91 among men and women, and the SMR of all cancers was 1.02 among men and 0.97 among women. Stomach cancer was the most frequent cancer among men (25.5%) and women (18.7%), followed by lung cancer among men (17.1%) and breast cancer among women (13.0%) (Table 5). The leading cause of death was cancer among men (35.0%) and cardiovascular disease among women (41.0%), and the second-leading cause of death was cardiovascular disease among men (33.0%) and cancer among women (25.7%) (Table 6). Among those who died of cancer, the first-, second-, and third-leading causes of death were cancer of the lung (21.9%), stomach (21.2%), and liver (14.4%) among men, and cancer of the stomach (18.7%), colon/rectum (13.2%), and lung (11.8%) among women.

Discussion

The Three-Prefecture Cohort Study, which had approximately 100,000 participants with consecutive follow-up for up to 15 years and a 90% response rate to the baseline questionnaire survey regarding participants' lifestyles, was one of the largest representative prospective, population-based cohort studies in Japan. The study areas were selected because they contained national air monitoring stations and the community-based cancer registry was conducted actively; this large-scale observation enabled us to determine not only all-cause mortality but also cancer incidence

among community residents. The association of air pollution and lung cancer mortality was reported previously.⁶ This report briefly describes the characteristics (e.g., smoking status, alcohol drinking status, and type of occupation) and endpoints among study participants by gender.

This study had several strengths. First, more than 100,000 participants answered a baseline questionnaire survey, and the response rate was approximately 90%. This response rate was similar to those of the JACC Study, which was launched in the mid-1980s,¹ and the JPHC Study, which was launched in the 1990s.² Many cohort studies in Japan have focused on residents in rural areas in order to conduct long-term follow-up.^{1,2} However, since this study included both urban and rural areas, findings from this cohort may help to evaluate the relationship between lifestyles and various diseases, irrespective of area. This study population was similar to the general population in cancer and mortality risks, with SIR and SMR close to 1.0.^{11,12} Considering the large sample size, the high questionnaire response rate, and adequate regional balance, we consider that the association between participants' lifestyles and endpoints measured in this study is generalizable to the whole population of Japan. Second, in contrast to other large-scale cohorts in Japan, the collection of detailed information on participants' occupation, such as the longest period of employment, is another strength of this study, and we will address the association between occupation and incidence and mortality of non-communicable

Table 6

Distribution of number of deaths by cause, gender, and age at baseline during 15-year follow-up.

| ICD10 | ICD9 | | Age at baseline, years | | | | | | | | | | Total | % | % |
|------------|-------------|--|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-----|--------|-------|-------|
| | | | 40–44 | 45–49 | 50–54 | 55–59 | 60–64 | 65–69 | 70–74 | 75–79 | 80–84 | ≥85 | | | |
| Men | | | | | | | | | | | | | | | |
| All causes | | | 320 | 506 | 960 | 1268 | 1407 | 1790 | 2054 | 1642 | 850 | 359 | 11,156 | 100.0 | |
| A00-B99 | 1–139.8 | Certain infectious and parasitic diseases | 22 | 11 | 38 | 40 | 31 | 46 | 35 | 28 | 10 | 6 | 267 | 2.4 | |
| C00-C97 | 140–208.9 | all cancer | 135 | 230 | 463 | 642 | 615 | 641 | 626 | 375 | 140 | 35 | 3902 | 35.0 | 100.0 |
| C15 | 150–150.9 | Esophagus | 15 | 13 | 22 | 41 | 32 | 27 | 26 | 9 | 7 | 0 | 192 | 4.9 | |
| C16 | 151–151.9 | Stomach | 28 | 39 | 104 | 126 | 120 | 137 | 151 | 84 | 29 | 11 | 829 | 21.2 | |
| C18 | 153–153.9 | Colon | 10 | 17 | 38 | 40 | 41 | 47 | 33 | 30 | 13 | 1 | 270 | 6.9 | |
| C19-20 | 154–154.9 | Rectum | 10 | 10 | 20 | 25 | 27 | 19 | 19 | 19 | 4 | 1 | 154 | 3.9 | |
| C22 | 155–155.9 | Liver and intrahepatic bile ducts | 16 | 52 | 107 | 127 | 80 | 76 | 60 | 29 | 14 | 2 | 563 | 14.4 | |
| C23 | 156 | Gall bladder | 0 | 4 | 4 | 4 | 10 | 9 | 6 | 4 | 0 | 1 | 42 | 1.1 | |
| C24 | 156.1–156.9 | Other and unspecified parts of biliary tract | 3 | 6 | 11 | 8 | 13 | 21 | 14 | 12 | 5 | 2 | 95 | 2.4 | |
| C25 | 157–157.9 | Pancreas | 9 | 14 | 21 | 39 | 41 | 36 | 33 | 23 | 6 | 2 | 224 | 5.7 | |
| C33-34 | 162–162.9 | Lung | 22 | 36 | 66 | 123 | 152 | 165 | 171 | 89 | 24 | 8 | 856 | 21.9 | |
| C61 | 185–185.9 | Prostate | 0 | 4 | 7 | 11 | 20 | 27 | 24 | 16 | 13 | 1 | 123 | 3.2 | |
| C64 | 189–189.1 | Kidney | 0 | 3 | 3 | 6 | 8 | 8 | 6 | 3 | 0 | 0 | 37 | 0.9 | |
| C65-67 | 189.2–189.4 | Urothelial tract | 0 | 0 | 1 | 4 | 2 | 3 | 3 | 1 | 0 | 0 | 14 | 0.4 | |
| C82-85 | 200–200.9 | Non-Hodgkin's | 3 | 2 | 9 | 12 | 11 | 10 | 13 | 8 | 2 | 2 | 72 | 1.8 | |
| | 202–202.9 | | | | | | | | | | | | | | |
| C90 | 203–203.8 | Multiple myeloma | 1 | 1 | 3 | 2 | 5 | 3 | 2 | 3 | 0 | 0 | 21 | | 0.5 |
| C92 | 205–205.9 | Myeloid leukemia | 3 | 3 | 6 | 5 | 8 | 6 | 4 | 2 | 1 | 2 | 40 | | 1.0 |
| E00-E89 | 240–279.9 | Endocrine, nutritional and metabolic diseases | 0 | 6 | 9 | 14 | 20 | 29 | 19 | 26 | 17 | 3 | 143 | 1.3 | |
| G00-G99 | 330–359.9 | Diseases of the nervous system | 1 | 5 | 6 | 9 | 12 | 18 | 10 | 8 | 3 | 0 | 72 | 0.6 | |
| I00-I99 | 390–459.9 | Diseases of the circulatory system | 76 | 121 | 242 | 304 | 407 | 578 | 772 | 644 | 364 | 173 | 3681 | 33.0 | |
| I20-I25 | 410–414.9 | Ischemic heart disease | 16 | 33 | 62 | 74 | 116 | 142 | 176 | 115 | 60 | 16 | 810 | | |
| I48 | 427.3 | Atrial fibrillation and flutter | 0 | 0 | 3 | 2 | 1 | 6 | 7 | 6 | 4 | 2 | 31 | | |
| I50 | 428–428.9 | Heart failure | 23 | 32 | 48 | 53 | 74 | 107 | 182 | 181 | 94 | 50 | 844 | | |
| I60-69 | 430–438.9 | Cerebrovascular disease | 26 | 42 | 87 | 130 | 143 | 216 | 308 | 270 | 166 | 88 | 1476 | | |
| I71 | 441–441.9 | Aortic aneurysm and dissection | 2 | 2 | 5 | 8 | 15 | 21 | 13 | 8 | 5 | 2 | 81 | | |
| J00-J99 | 460–519.9 | Diseases of the respiratory system | 4 | 14 | 41 | 76 | 134 | 255 | 351 | 299 | 161 | 59 | 1394 | 12.5 | |
| J10-J18 | 480–487.9 | Influenza | 1 | 8 | 15 | 46 | 68 | 139 | 228 | 198 | 113 | 40 | 856 | | |
| J43 | 492 | Emphysema | 0 | 0 | 5 | 5 | 5 | 22 | 19 | 14 | 4 | 5 | 79 | | |
| K00-K93 | 520–579.9 | Diseases of the digestive system | 21 | 39 | 63 | 61 | 59 | 69 | 62 | 59 | 27 | 6 | 466 | 4.2 | |
| K74 | 571.5–571.6 | Fibrosis and cirrhosis of liver | 7 | 14 | 38 | 26 | 22 | 17 | 12 | 10 | 6 | 0 | 152 | | |
| N00-N99 | 580–629.9 | Diseases of the genitourinary system | 4 | 7 | 12 | 29 | 36 | 37 | 57 | 53 | 25 | 8 | 268 | 2.4 | |
| N17-N19 | 584–586 | Acute kidney failure and chronic kidney disease | 3 | 7 | 11 | 21 | 32 | 28 | 48 | 43 | 17 | 2 | 212 | | |
| R00-R99 | 780–799.9 | Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified | 7 | 3 | 5 | 15 | 17 | 33 | 51 | 80 | 67 | 56 | 334 | 3.0 | |
| R54 | 797 | Age-related physical debility | 1 | 0 | 0 | 1 | 1 | 11 | 15 | 57 | 52 | 55 | 193 | | |
| S00-T88 | 800–999.9 | External causes | 42 | 56 | 60 | 57 | 53 | 43 | 41 | 35 | 21 | 5 | 413 | 3.7 | |
| | | Others | 8 | 14 | 21 | 21 | 23 | 41 | 30 | 35 | 15 | 8 | 216 | 1.9 | |
| Women | | | | | | | | | | | | | | | |
| All causes | | | 181 | 301 | 446 | 662 | 946 | 1365 | 1712 | 1648 | 1157 | 666 | 9084 | 100.0 | |
| A00-B99 | 1–139.8 | Certain infectious and parasitic diseases | 6 | 7 | 21 | 24 | 36 | 31 | 38 | 33 | 21 | 4 | 221 | 2.4 | |
| C00-C97 | 140–208.9 | all cancer | 98 | 170 | 211 | 286 | 325 | 410 | 404 | 278 | 115 | 34 | 2331 | 25.7 | 100.0 |
| C15 | 150–150.9 | Esophagus | 0 | 0 | 2 | 6 | 2 | 4 | 8 | 5 | 3 | 0 | 30 | 1.3 | |
| C16 | 151–151.9 | Stomach | 15 | 29 | 35 | 49 | 51 | 74 | 80 | 65 | 31 | 7 | 436 | 18.7 | |
| C18 | 153–153.9 | Colon | 5 | 16 | 22 | 27 | 25 | 30 | 46 | 33 | 10 | 5 | 219 | 9.4 | |
| C19-20 | 154–154.9 | Rectum | 3 | 10 | 13 | 16 | 13 | 19 | 16 | 10 | 9 | 2 | 111 | 4.8 | |
| C22 | 155–155.9 | Liver and intrahepatic bile ducts | 4 | 14 | 14 | 26 | 40 | 38 | 30 | 11 | 8 | 2 | 187 | 8.0 | |
| C23 | 156 | Gall bladder | 1 | 2 | 7 | 9 | 8 | 19 | 15 | 9 | 1 | 0 | 71 | 3.0 | |
| C24 | 156.1–156.9 | Other and unspecified parts of biliary tract | 3 | 6 | 8 | 7 | 13 | 21 | 14 | 16 | 7 | 2 | 97 | 4.2 | |
| C25 | 157–157.9 | Pancreas | 5 | 6 | 12 | 32 | 25 | 40 | 30 | 18 | 6 | 2 | 176 | 7.6 | |
| C33-34 | 162–162.9 | Lung | 11 | 12 | 17 | 36 | 38 | 55 | 57 | 33 | 11 | 5 | 275 | 11.8 | |
| C50 | 174–175.9 | Breast | 23 | 29 | 22 | 16 | 22 | 16 | 11 | 8 | 3 | 0 | 150 | 6.4 | |
| C53 | 180–180.9 | Cervi uteri | 5 | 4 | 1 | 4 | 7 | 8 | 5 | 4 | 0 | 0 | 38 | 1.6 | |
| C54 | 182–182.9 | Corpus uteri | 1 | 4 | 4 | 3 | 0 | 3 | 7 | 0 | 0 | 0 | 22 | 0.9 | |
| C55 | 184–184.9 | Uterus, part unspecified | 0 | 0 | 0 | 1 | 2 | 1 | 1 | 0 | 2 | 0 | 7 | 0.3 | |
| C56 | 183–183.9 | Ovary | 8 | 9 | 15 | 10 | 8 | 9 | 11 | 6 | 4 | 0 | 80 | 3.4 | |
| C64 | 189–189.1 | Kidney | 1 | 0 | 0 | 3 | 0 | 1 | 7 | 1 | 3 | 0 | 16 | 0.7 | |
| C65-67 | 189.2–189.4 | Urothelial tract | 0 | 0 | 2 | 1 | 4 | 1 | 2 | 0 | 0 | 0 | 10 | 0.4 | |
| C82-85 | 200–200.9 | Non-Hodgkin's | 1 | 2 | 4 | 8 | 9 | 9 | 3 | 6 | 4 | 1 | 47 | 2.0 | |
| | 202–202.9 | | | | | | | | | | | | | | |
| C90 | 203–203.8 | Multiple myeloma | 0 | 1 | 3 | 4 | 4 | 5 | 8 | 4 | 1 | 0 | 30 | | 1.3 |
| C92 | 205–205.9 | Myeloid leukemia | 2 | 5 | 3 | 4 | 4 | 6 | 1 | 2 | 0 | 0 | 27 | | 1.2 |
| E00-E89 | 240–279.9 | Endocrine, nutritional and metabolic diseases | 2 | 4 | 5 | 12 | 18 | 20 | 37 | 29 | 15 | 3 | 145 | 1.6 | |
| G00-G99 | 330–359.9 | Diseases of the nervous system | 3 | 2 | 8 | 4 | 11 | 13 | 9 | 12 | 4 | 0 | 66 | 0.7 | |
| I00-I99 | 390–459.9 | Diseases of the circulatory system | 33 | 65 | 112 | 171 | 322 | 543 | 753 | 780 | 600 | 343 | 3722 | 41.0 | |
| I20-I25 | 410–414.9 | Ischemic heart disease | 4 | 9 | 24 | 39 | 73 | 127 | 134 | 123 | 89 | 32 | 654 | | |
| I48 | 427.3 | Atrial fibrillation and flutter | 0 | 0 | 0 | 2 | 0 | 3 | 7 | 8 | 2 | 1 | 23 | | |

Table 6 (continued)

| ICD10 | ICD9 | | Age at baseline, years | | | | | | | | | | Total | % | % |
|---------|-------------|--|------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-----|-------|------|---|
| | | | 40–44 | 45–49 | 50–54 | 55–59 | 60–64 | 65–69 | 70–74 | 75–79 | 80–84 | ≥85 | | | |
| I50 | 428–428.9 | Heart failure | 9 | 8 | 20 | 28 | 71 | 124 | 164 | 218 | 173 | 118 | 933 | | |
| I60–I69 | 430–438.9 | Cerebrovascular disease | 12 | 33 | 50 | 81 | 130 | 218 | 335 | 337 | 251 | 150 | 1597 | | |
| I71 | 441–441.9 | Aortic aneurysm and dissection | 1 | 1 | 0 | 1 | 5 | 8 | 12 | 8 | 2 | 0 | 38 | | |
| J00–J99 | 460–519.9 | Diseases of the respiratory system | 7 | 12 | 20 | 47 | 81 | 111 | 197 | 221 | 138 | 75 | 909 | 10.0 | |
| J10–J18 | 480–487.9 | Influenza | 1 | 4 | 8 | 25 | 44 | 72 | 133 | 149 | 98 | 67 | 601 | | |
| J43 | 492 | Emphysema | 0 | 0 | 0 | 1 | 2 | 1 | 1 | 4 | 3 | 2 | 14 | | |
| K00–K93 | 520–579.9 | Diseases of the digestive system | 9 | 9 | 24 | 39 | 38 | 62 | 68 | 68 | 54 | 26 | 397 | 4.4 | |
| K74 | 571.5–571.6 | Fibrosis and cirrhosis of liver | 5 | 5 | 10 | 18 | 17 | 22 | 22 | 10 | 2 | 0 | 111 | | |
| N00–N99 | 580–629.9 | Diseases of the genitourinary system | 3 | 3 | 9 | 19 | 23 | 45 | 65 | 52 | 43 | 17 | 279 | 3.1 | |
| N17–N19 | 584–586 | Acute kidney failure and chronic kidney disease | 3 | 3 | 8 | 17 | 18 | 33 | 50 | 38 | 29 | 16 | 215 | | |
| R00–R99 | 780–799.9 | Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified | 2 | 3 | 2 | 11 | 11 | 33 | 51 | 109 | 119 | 141 | 482 | 5.3 | |
| R54 | 797 | Age-related physical debility | 0 | 0 | 0 | 0 | 2 | 16 | 28 | 87 | 112 | 130 | 375 | | |
| S00–T88 | 800–999.9 | External causes | 11 | 18 | 15 | 31 | 50 | 52 | 46 | 26 | 21 | 11 | 281 | 3.1 | |
| | | Others | 7 | 8 | 19 | 18 | 31 | 45 | 44 | 40 | 27 | 12 | 251 | 2.8 | |

diseases in the future using this cohort data. Third, the use of community-based cancer incidence data from a cohort of 100,000 participants was also a strength of this study, because there are few available analyses of cancer incidence data from large-scale cohort studies in Japan. Fourth, this cohort can be pooled with other large-scale cohorts in Japan (e.g., the JACC Study,¹ the JPHC Study,² or the Ohsaki Cohort¹³) and serve to provide new findings from Japan.

This study has several limitations. First, this registry was launched in the 1980s and its follow-up of participants was completed in 2000. The associations between participants' lifestyles and endpoints might differ from those since 2000, because lifestyles diversify with the times. Second, in cohort studies, non-questionnaire responders had more unfavorable lifestyles than responders^{2,14–16} and were less likely to join the health check-ups.² However, the overall response rate in this cohort was almost 90%, and we consider that the impact of differences between responders in cities and those in towns would be small. Furthermore, the numbers of delivered questionnaires in Sendai City and Osaka City were fewer than those in other cities/towns, because residents' local organizations did not cover the entire community and could not deliver questionnaires in the whole region. Therefore, the representativeness would be weaker in these areas than in other areas. Third, we could not evaluate the energy intake or nutrient consumption of participants because the Three-Prefecture Cohort Study used a food frequency questionnaire with a small number of items.

Conclusions

The Three-Prefecture Cohort Study was conducted from the 1980s to 2000 and is one of the largest representative prospective population-based cohort studies in Japan. This study enabled us to reveal the association of multiphasic lifestyle factors with cancer incidence and mortality in a single cohort. It will also allow us to conduct a pooled analysis in combination with other large-scale cohorts, which will be of considerable help in gaining insights into the epidemiology of non-communicable diseases in Japan.

Conflicts of interest

None declared.

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